

P009 Proton-assisted amino acid transporters activate the TOR/S6 kinase signalling cascade from intracellular compartments

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The mechanisms by which extracellular amino acids activate mTOR signalling in multicellular organisms are still poorly characterised. We have highlighted the proton-assisted (PAT/SLC36) amino acid transporters as having a uniquely potent effect on PI3K/Akt signalling and TOR/S6-kinase-mediated growth from *in vivo* analysis in *Drosophila*. Using GFP-tagged functional versions of the two characterised fly PATs, CG1139 and PATH, we show that the PATs are located in endosomal and lysosomal compartments, as well as at the cell surface. Intriguingly, staining with an antibody against activated, phosphorylated S6K, reveals that these intracellular compartments also activate TOR. When PATs are relocalised within the cell, for example by the increased bulk endocytosis caused by overexpressing the PI3K/Akt target Rheb, activated S6K also localises to the new PAT-containing compartments. These data suggest that PATs control TOR signalling from both the plasma membrane and also from endosomal/lysosomal compartments, perhaps using the recently identified RAG-dependent TOR-regulatory system. We propose that this mechanism could provide a route by which tumour cells with activated PI3K/Akt out-compete more normal cells in nutrient- and growth factor-deprived conditions often associated with cancer.